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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/581,106	01/30/2001	Frederick M. Ausubel	00786/362002	2344

7590
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12/19/2002

EXAMINER

TUNG, JOYCE

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 12/19/2002

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/581,106

Applicant(s)

Ausubel et al.

Examiner

Joyce Tung

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Nov 18, 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 and 12-20 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 and 12-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

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DETAILED ACTION

In light of the following new ground of rejection, the finality of the Office action mailed 6/18/2002 is withdrawn.

1. Applicant's arguments with respect to claims 1-10 and 12-20 under 35 U.S.C. §112, second paragraph, 102(b) anticipated by Sorenson (5,496,699) and 103(a) over Sorenson (5,496,699) in view of Mullis et al. have been considered but are moot in view of the new ground(s) of rejection.

NEW GROUNDS OF REJECTIONS

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. claims 2-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
 - a. claims 2-5 are vague and indefinite because it is unclear what is meant by the language "different ranges of specificity" in claim 2. Further, it is unclear what is meant by the language "3000-fold range of specificity". Does it mean that the specificity is within the range of 3000 nucleotides sequence long. It is suggested to clarify uncertainty.

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Applicants argue that the modifier "3000-fold" means that the highest concentration at which a target sequence is preferentially amplified is 3000 times the lowest concentration at which the target sequence is preferentially amplified. This limitation is not in the claim language. Thus, the rejection is remained.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. claims 1, 6-7, 9, 12, and 14-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Newton et al. (5,595,890) in view of Sorenson (5,496,699).

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Newton et al. disclose a method for detecting the presence or absence of one or more variant nucleotide sequences. The method applies a diagnostic primer which is substantially complementary to a diagnostic portion of a target base sequence (See the Abstract). The diagnostic primer has the same structure as the one of said first pair of primer and one of said second pair of primer (See column 4, lines 33-53 and column 29, lines 18-31). Newton et al. also disclose that 6 nucleotides adjacent to the terminal mismatch may be altered to introduce further mismatching (See column 12, lines 27-29) (as recited in claim 6). The primers can be labeled (See column 14, lines 40-43). Newton et al. also disclose constructing a kit including the primers (See column 8, lines 62 to column 9, lines 1-34).

Newton et al. do not disclose more than one pair of PCR primers are used in the method. However, Newton et al. indicate that the method can be used in detecting the presence or absence of more than one suspected variant nucleotide in the same sample (Column 3, lines 42-44). This teachings would have motivated one of ordinary skill in the art at the time of the instant invention to apply more than one pair of PCR primers for the detection.

Nevertheless, Sorenson discloses a method of detecting mutated genes and oncogenes via amplification (See the abstract) in an allele specific manner to distinguish a normal gene sequence from a mutated gene sequence present in the sample (See column 2, lines 19-23). The method applies four primer pairs including a set of four allele-specific first primers complementary to the gene sequence contiguous with the site of the mutation on the first strand and at 3' nucleotide it is complementary to one of three possible mutations which can occur at

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this known position (See column 2, lines 27-33). These primers are unique with respect to each other and differ only at the 3' nucleotide (See column 2, lines 29-33) (as recited in the limitations of claims 1-2 and 14). Sorenson further suggests that some mismatches 3-6 nucleotides back maybe made and the 3' terminal nucleotide must remain the same (See column 7, lines 19-24). The amplified product can be separated from the reaction mixture by adsorption to avidin or streptavidin attached to a solid support (See column 10, lines 33-44) (as recited in the limitations of claim 12). The method of this invention may embodied in diagnostic kits including reagents for the isolation of DNA as well as sets of primers used in the detection and reagents used in the amplification (See column 9, lines 29-41) (as recited in the limitations of claims 15-20). The disclosure of Sorenson et al. also involves labeled primers for the detection of the amplified product (See column 8, lines 21-25) (as recited in the limitations of claim 9).

One of ordinary skill in the art at the time of the instant invention would have been motivated to modify the method of Newton et al. by applying more than one pair of PCR primers as taught by Sorenson et al. because the motivation is that when the mutated allele is present, the primer pair including the allele-specific primer will amplify efficiently and yield a detectable product (Column 5, lines 14-19) and Sorenson also addresses that where the mutation may exist at one or two locations, eight pair of oligonucleotide primers may be used (See column 5, lines 21-22). Thus, it would have been prima facie obvious to carry out the method as claimed.

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6. Claims 10 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Newton et al. (5,595,890) in view of Sorenson (5,496,699) as applied to claims 1, 6-7, 9, 12, and 14-20 above, and further in view of Mullis et al. (4,965,188).

The teachings of Newton et al. and Sorenson are set forth in section 5 above and Newton et al. and Sorenson do not disclose using a hybridization tag, but Sorenson et al. indicate that the amplified products are attached to a solid support by adsorption to avidin or streptavidin (See column 10, lines 33-38). This is inherent that there is a binding partner for the immobilization (as recited in the limitations of claim 12)

Mullis et al. disclose detecting the amplified product by using sequence specific oligonucleotide affixed to a membrane (See column 5, lines 3-12). Mullis et al. also disclose using a labeled oligonucleotide probe for mutation detection (See column 4, lines 43-46 and lines 60-65).

One of ordinary skill in the art at the time of the instant invention would have been motivated to modify the method of Newton et al. by using a sequence-specific labeled oligonucleotide for the detection because by using the sequence-specific labeled oligonucleotide probe, it increases the specificity for mutation detection as disclosed by Mullis et al. that the process is especially useful in detecting nucleotide variations with only very small amounts (See column 38, lines 25-30). It would have been prima facies obvious to carry out the method as claimed.

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Allowable Subject Matter

7. Claims 8 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

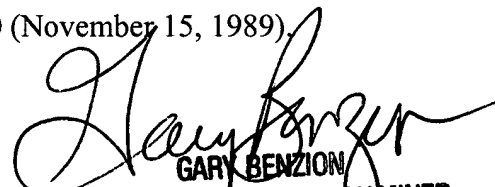
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

December 8, 2002


GARY BENZION
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600